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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Mads Grunberg

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10/26/2006

EXAMINER

WHALEY, PABLO S

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NEW YORK, NY 10104

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/016,616	Applicant(s) GRUENBERG ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-16 is/are pending in the application.
- 4a) Of the above claim(s) 2,5,7 and 9-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,7 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

CLAIMS UNDER EXAMINATION

Claims herein under examination are 1, 3, 4, and 7-8, as they read upon the elected Species I-B (an optimization routine). Claim 6 has been canceled. Claims 2, 5, and 9-16 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied, as necessitated by amendment. They constitute the complete set presently being applied to the instant application.

PRIORITY

Acknowledgment is made of applicant's claim for foreign priority based on European Patent Office (EPO) Application No. 000123710.6, filed on 10/31/2000. However, priority is not granted as the priority document was apparently lost as there is no record of one in the IFW file. Applicant is kindly requested to file another copy of the above priority document before or with the filing of a response to this office action. It is noted that the date of filing will be the date of the filing of the first copy (original). The Examiner wishes to apologize for the inconvenience to the applicant.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 7, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These rejections are necessitated by amendment.

Claim 1 has been amended to recite the limitation "a ratio....is treated as a separate control variable but is adjusted simultaneously." While applicant's have corrected the unclarity regarding the elements being "controlled for", it is now unclear if the above limitation is intended to be an active method step (e.g. directed to treatment and adjustment of a ratio), or a further limitation of the claim method. If the later, it is unclear as to the intended meaning of "is treated...but adjusted" such that one skilled in the art would know in what way said ratio "is treated as a separate control variable but is adjusted simultaneously." Is the ratio being used to "adjust" the amount of each nutrient? Clarification is requested. The Examiner has interpreted this limitation broadly for purposes of applying prior art.

Claim 1 has been amended to recite the limitation "a separate control variable." There is lack of antecedent basis for this limitation, as there is no previous recitation of any limitation directed to a "control variable." It is noted that claim 4 recites generating control variables. Correction is requested.

Claim 4 recites the limitation "an actual pulse response time Δt_i ." There is insufficient antecedent basis for this limitation. It is noted that claim 4 previously recites "response times." Correction is requested.

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Claim 4 recites the limitation "a response time Δt_{i-1} ." There is insufficient antecedent basis for this limitation. It is noted that claim 4 previously recites "response times." Correction is requested.

Claim 4 recites the limitation "a respective other complex nutrient." It is unclear as to the intended meaning of "a respective other" in this context. Clarification is requested.

Claims 1, 3, 4, 7, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 1 now recites "adjusting the amount...with an optimization routine, wherein a ratio....is treated as a separate control variable but is adjusted simultaneously." The omitted essential steps appear to be: (i) calculation of control variable(s), and (ii) calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, since the instant claims do not indicate which calculations of the preceding steps would indicate a ratio between the feed concentration and the total quantity. Clarification is requested.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1, 3, 4, 7, and 8 are rejected under 35 U.S.C. 102 (b) as being anticipated by Fleury et al. (Advances in Bioprocess Engineering, 1994, p.313-320).

Applicant's arguments, filed 08/21/2006, that Fluery et al. do not teach "a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients is treated as a separate control variable" are not deemed to be persuasive. This rejection is reiterated.

Claim 1, step (c), now recites "adjusting the amount...with an optimization routine, wherein a ratio....is treated as a separate control variable but is adjusted simultaneously." It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, therefore the Examiner has interpreted this limitation broadly.

Fleury et al. clearly teach feed concentrations for biomass (X), sorbose (p), sorbitol (s_1), and yeast (s_2), etc. (i.e. complex nutrients) obtained over time [Fig. 1]. Webster's dictionary (10th edition) defines "ratio", *inter alia*, as the relationship in quantity, size, or amount between two or more things, therefore each of the above concentrations taught by Fluery et al. is clearly a teaching for a "ratio" between the respective complex nutrient and the total biomass of the complex nutrients, as in claim 1. Fluery et al. also teach concentrations used as separate model parameters (i.e. control variables) [Table 3]. Fluery et al. also teach an optimization equation comprising an input ratio of quantitative measurements for sorbose and sorbitol (i.e. Q_{sens}) [p.317, EQN (22)] and related pulse response times [Fig. 4], as in claim 1. Fluery et al. also teach a ratio between lowest and highest eigenvalues for D-sorbitol conversion to L-sorbose for system optimization and partitioning [p.317, Col. 2, ¶ 2], which also equates to a ratio treated as a separate control variable as in claim 1. Furthermore, Fluery et al. teach sorbose (p) and

sorbitol (s_1) measurements containing delays that are included into the simulation after an actualization cycle [p.318, Simulations and Results, Section 1], which is a teaching for Δt delays and previous cycles as in amended claim 4.

For the above reasons, and for reasons set forth in the previous office action, the Examiner maintains that Fluery et al. anticipates instant claims 1, 3, 4, 7, and 8.

Claims 1 and 3 are rejected under 35 U.S.C. 102 (a) as being anticipated by Miskiewicz et al. (Biotechnology Letters, 22: 1685-1691, 2000).

Applicant's arguments, filed 08/21/2006, that Miskiewicz et al. do not teach "a ratio between the feed concentration of the complex nutrients and the total quantity of the complex nutrients is treated as a separate control variable" are not deemed to be persuasive. This rejection is maintained for the reasons set forth below.

Claim 1, step (c), now recites "adjusting the amount...with an optimization routine, wherein a ratio....is treated as a separate control variable but is adjusted simultaneously." It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, therefore the Examiner has interpreted this limitation broadly.

Miskiewicz et al. clearly teach calculation of consecutive nutrient dosage based on multiple inputs [p.1686, col. 2, lines 24-26] and an optimization routine using a fuzzy logic controller with nutrient feed input variables to optimize yield (i.e. output) [p. 1685, col. 2, paragraph 2; and p.1686, col. 1, paragraph 1], and define relationships between input concentrations and the yield control variables [Fig. 4, 5, and 6]. Webster's dictionary (10th edition) defines "ratio", *inter alia*, as the relationship in quantity, size, or amount between two or more things. Therefore, the

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above "relationship" taught by Miskiewicz et al. is a teaching for a "ratio" between the respective complex nutrient and the yield (i.e. quantity) of the complex nutrients, as in claim 1.

For the above reasons, and for reasons set forth in the previous office action, the Examiner maintains that Miskiewicz et al. anticipates instant claims 1 and 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 4, and 7-8 are rejected under 35 U.S.C. 103(a) as being obvious by Kurokawa et al. (Biotechnology And Bioengineering, Vol. 44, No. 1, 1994), in view of Fleury et al. (Advances in Bioprocess Engineering, 1994, p.313-320) and Johnson et al. (US Pat. No. 6,792,336; Filed: May 13, 1999).

Applicant's arguments, filed 08/21/2006, that (i) Kurokawa et al. do not teach "a ratio between the feed concentration of the complex nutrients and the total quantity of the complex

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nutrients is treated as a separate control variable", and that (ii) the Examiner has not provided why one skilled in the art would modify the disclosure of Kurokawa et al. using Johnson et al. and Fluery et al. to arrive at the claimed method are not deemed to be persuasive. This rejection is maintained for the reasons set forth below.

Regarding (i): Claim 1, step (c), now recites "adjusting the amount...with an optimization routine, wherein a ratio...is treated as a separate control variable but is adjusted simultaneously." It is noted that claim 1 does not require the calculation of a ratio of feed concentration of the complex nutrients to the total quantity of the complex nutrients, therefore the Examiner has interpreted this limitation broadly. As set forth in the previous office action, Kurokawa et al. teach a method for simultaneously controlling glucose and glutamine concentrations comprising the following:

- An adaptive control algorithm (i.e. optimization routine) for adjusting the feed rates from real-time data at every sampling time [p.98, col. 2, lines 29-32], as in amended claim 1(a) and the elected species.
- Independent model parameters comprising ratios of feed concentrations [EQNs (9)-(12)], as in amended claim 1(c).
- Generation of time-variant flow charts and response times based on three control algorithms comprising control variables [Fig. 2 and 3], as in amended claim 4(a).
- Input variables comprising distinct response times represented as quotients [p.97, Equation (7)], as in amended claim 4(c).

Regarding (ii): The Examiner wishes to apologize for the confusion regarding the use of Johnson et al., and would like to provide clarification:

As set forth in the previous office action, it was noted that Kurokawa et al. do not specifically teach the use of a "microorganism", as in claim 7 and 8. Fleury et al. teach a multi-feed system and modeling and control strategies for the transformation of D-sorbitol to L-Sorbose using the microorganism *Gluconobacter oxydans* (i.e. *suboxydans*) [p.313, col. 1, paragraph 1], as required by claims 7 and 8.

As Kurokawa et al. suggest the use of such control models with fermentation processes involving microorganisms [p.95, col. 2, paragraph 3], this was the primary motivation to combine the optimization method of Kurokawa et al. with the use of *Gluconobacter oxydans* (i.e. *suboxydans*) as taught by Fluery et al. The intended use of Johnson et al. was to support a reasonable expectation for one of ordinary skill in the art successfully combining the optimization method of Kurokawa et al. with the use of the microorganism *Gluconobacter oxydans*, as taught by Fluery et al., as Johnson et al. teaches both optimization routines for nutrient mixtures [29] and [31], as well as the use of minerals-processing microorganisms [9]. Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to combine the optimization method of Kurokawa et al. with the use of *Gluconobacter oxydans* (i.e. *suboxydans*) as taught by Fluery et al. resulting in the practice of the instant claimed invention with a reasonable expectation of success.

As the examiner maintains that Kurokawa et al. teach the limitations of claims 1, 3, 4, and 7-8, as set forth in the previous office action and maintained above, he also maintains that Kurokawa et al. combined with Fluery et al. and Johnson et al. make obvious claims 1, 3, 4, and 7-8 for the reasons and motivation previously set forth.

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CONCLUSION

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

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Lois A. Clow
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10/24/06